

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
BOCK et al.	)	Art Unit: Unassigned
Application No. 10/516,662	)	Examiner: Unassigned
Filing Date: June 2, 2003	)	Confirmation No. 2888
For VARIANTS OF ANTITHROMBIN III	, ,	

#### INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

NEEDLE & ROSENBERG, P.C. Customer Number 23859

Sir:

Pursuant to the requirements of 37 C.F.R. § 1.56, submitted herewith on the accompanying Information Disclosure Statement List is a listing of documents known to Applicants and/or their attorneys. In accordance with 37 CFR 1.98 (a)(2), copies of any cited U.S. Patent or U.S. Patent Publication documents are not enclosed.

In accordance with the provisions of M.P.E.P. § 2001.06(b) and 37 C.F.R. § 1.98(b)(3), Applicants would like to bring to the attention of the Examiner the existence of the co-pending patent application(s) identified below, which were filed in the United States Patent and Trademark Office:

Application No.	<b>Date Filed</b>	<u>Inventors</u>	Attorney Docket No.
PCT/US05/00843	January 10/2005	Bock et al.	21101.0054P1

In accordance with the requirements of 37 C.F.R. § 1.98(a)(2)(iii), a copy of the abovereferenced application specification(s), including the claims and drawings thereof, is enclosed.

#### ATTORNEY DOCKET NO. 21101.0021U2 Application No. 10/516,662

Consideration of the cited documents and making the same of record in the prosecution of the above-referenced application are respectfully requested.

No fee is believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

Christopher L. Curfman, JD, PhD

Registration No. 52,787

NEEDLE & ROSENBERG, P.C. Customer Number 23859 (678) 420-9300 (678) 420-9301 (fax)

#### CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.

Christopher L. Curfman

Date



# Res'd PCT/PTO 25 NOV 2005

ATTORNEY DOCKET NO. 21101.0021U2 APPLICATION NO. 10/516,662 SHEET 1 OF 4

	- Zarei	FICE /	···		T			omplete if K	nown
INFORMATION DISCLOSURE STATEMENT			Appl	ication Number		16,662	NIO WILL		
LIST					Filing	Filing Date June 2, 200		2, 2003	
	2.01					Named Inventor	Bock	et al.	
	(Use as m	any sheets as necessary	/)		ļ	p Art Unit		signed	
						niner Name		signed	
							Ulla	ssigned	
	Louis No.	I 8			PATEN	T DOCUMENTS	LOless	l Cubalaa	Triing Date of
Examiner's Initials	Cite No.	Document No.		Date		Name	Class	Subclas	Filing Date (if appropriate
	A1	6,878,813	04/1		<del></del>	et al.	530	393	12/11/01
	A2	5,204,253	04/2		Kato	ord et al.	435 530	459 393	
<u> </u>	A3	5,420,252	04/0			en al. emeissl et al.	435	226	
	A4	5,618,713 5,700,663	12/2			emeissi et al.	435	69.6	
	A5 A6	5,843,705	12/2			lio et al.	800	7	
	A0	1 5,645,705	1			ENT DOCUMEN	<del></del>	1.	
Examiner's	Cite No.	Foreign Patent Docu	_	Dat		Nan		Тт	ranslation
Initials	Cite No.	Country Code-Number-Kir							Yes/No
<b>)</b> .	A7	EP 0 568 833 A1		08/04/9		Kato et al.			
	A8	WO 90/09737		07/09/9		Blood Research	Center		
	A9	WO 91/00291		01/10/9		Akzo			
	A10	WO 95/05853		03/02/9	-	Carson et al.			**** * <u>**</u> *****
				NON-	PATEN	IT DOCUMENTS			
Examiner's Initials	Cite No.		Non-F	Patent Citat	ions (ind	ude Author, Title, Publisher	Relevant Pa	iges, Date and	Place of Publication)
	A11	Backovic and Gettins, "Insight into residues critical for antithrombin function from an expanded database of sequences that includes frog, turtle and ostrich antithrombins." J. Proteome Res. <b>2002</b> 1:367-373.  Bayston et al. "Familial overexpression of beta antithrombin caused by an Asn135Thr substitution." Blood							
_	A 12								
	A12	<b>1999</b> 93:4242-7.		·					
	A13	Bick et al. "Antithr 73(4):577-83.	ombin	III patter	ns in d	isseminated intra	vascula	coagula	tion." Am. J. Clin. Pathol. 1980
	A14	Blauhut et al. "Substitution of antithrombin III in shock and DIC: a randomize			zed study." Thromb. Res. 1985				
	A15	39(1):81-9.	ed an	d inactiv	ated ar	tithrombin III in b	ronchoa	lveolar la	vage (RAL) samples from acute
	Ais	Bock et al., "Cleaved and inactivated antithrombin III in bror respiratory distress (ARDS) and at-risk for ARDS patents," Respir. Crit. Care Med., 2001, A63. (Poster Abstract)  Bock et al. "Cloning and expression of the cDNA for human 10(24):8113-25.			at-risk	for ARDS patents			
	ļ							aramahin I	II." Niveleie Aside Des 4092
	A16								
	A17	Brennan et al. "Physiological variant of antithrombin-III lacks carbohydrate sidechain at Asn 135." FEB: Lett. 1987 219(2):431-6.				sidechain at Asn 135." FEBS			
	A18	Buller and Cate, "Acquired antithrombin III deficiency: laboratory diagnosis, incidence, clinical implication and treatment with antithrombin III concentrate." Am. J. Med. 1989 87(3B):44S-48S.							
	A19	Carlson et al. "Comparison of the behavior in vivo of two molecular forms of antithrombin III." Biochem. J. 1985 225:557-64.  Carrell and Owen, "Plakalbumin, alpha 1-antitrypsin, antithrombin and the mechanism of inflammatory							
	A20					mechanism of inflammatory			
		thrombosis." Nature. 1985 317(6039):730-2.  A21 Cohen et al. "In vivo inactivation of antithrombin III is promoted by heparin during cardiopulmonary bypass." J. Invest. Surg. 1992 5:45-9.							
<u> </u>	A21								
	A22	Cunningham et al. "Development of an elastase-resistant antithrombin through mutagenesis at P4." Blood. 1995 86(10 Supp.):375A. (Abstract)							

Examiner Signature:	Date Considered:			
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not				

## Res'd PUTIFTO 25 NOV 2005

ATTORNEY DOCKET NO. 21101.0021U2 APPLICATION NO. 10/516,662 SHEET 2 OF 4

			Complete if Known		
INFORMATION	I DISCLOSURE STATEMENT	Application Number	10/516,662		
	LIST	Filing Date	June 2, 2003		
		First Named Inventor	Bock et al.		
(Use a	s many sheets as necessary)	Group Art Unit	Unassigned		
		Examiner Name	Unassigned		
A2	2 Cunningham et al "Impact of mi		position on the reation of antithrombin with		
, A2	thrombin and elastase." Thromb				
A2	4 Damus and Wallace, "Immunolo	gic measurement of antith	rombin III-heparin cofactor and alpha2		
	<b>1975</b> 6(1):27-38.	•	nd hepatic failure coagulopathy." Thromb Res.		
A2	deAgostini et al. "Localization of endothelium: Antithrombin bindii 111:1293-1304.	anticoagulantly active hering on cultured endothelial	paran sulfate proteoglycans in vascular cells and perfused rat aorta." J. Cell Biol. 1990		
A2	a concentrate containing F XIII a	and native von Willebrand	Il treatment with antithrombin III concentrate and factor." J. Intern. Med. 1989 225(1):21-7.		
A2	pneumoniae induced sepsis." The	romb Haemost. 1993 69(			
, A2	migration by the serpin antithron	nbin III." Blood <b>2001</b> 97:10			
A2	endotoxemia or bacteremia." An	n. J. Med. <b>1989</b> 87:27S-33	n animal models of fulminant Eschericia coli S.		
A3	the Escherichia coli endotoxemi	Emerson et al. "Protection against disseminated intravascular coagulation and death by antithrombin-III the Escherichia coli endotoxemic rat." Circ Shock. 1987 21(1):1-13.			
A3	human antithrombin III by express 1995 310:323-30.	Ersdal-Badju et al. "Elimination of glycosylation heterogeneity affecting heparin affinity of recombinant human antithrombin III by expression of a beta-like variant in baculovirusinfected insect cells." Biochem. J. 1995 310:323-30.			
A3	disseminated intravascular coag	Fourrier et al. "Double-blind, placebo-controlled trial of antithrombin III concentrates in septic shock with disseminated intravascular coagulation." Chest. 1993 104(3):882-8.			
A3	<b>1980</b> 255(11):5090-3.		ion of human antithrombin III." J. Biol. Chem.		
A3	4 Frebelius et al. "Thrombin inhibit AT-beta." Thromb. Vasc. Biol. 19	tion by antithrombin III on 1 996 16:1292-7.	the subendothelium is explained by the isoform		
A3		bits thrombin-induced pro	iferation in human arterial smooth muscle cells."		
A3		concentrate as adjuvant in	DIC treatment. A pilot study in 9 severely ill		
A3		n and fibrinolytic factors a	nd their inhibitors in critically ill patients."		
A3	8 Hoffmann et al. "Antithrombin ef by its interaction with microvasce		d microcirculatory disorders are mediated mainly re Med. <b>2002</b> 30:218-25.		
A3	<b>2000</b> 106(7):873-878.		e results in embryonic lethality." J. Clin. Invest.		
A4	activates antithrombin III for thro 277:24460-5.	mbin inhibition but not fac	with underlying glutamic acid-255 partially tor Xa inhibition." J. Biol. Chem. <b>2002</b>		
A4	Physiol Chem. 1981 362(2):103-	-12.	olated human antithrombin III." Hoppe Seylers Z		
A4	cytokines, and soluble adhesion 2):19-32.	molecules in acute inflam	therapy on the release of cellular proteinases, mation." Semin Hematol. 1995 32(4 Suppl		
. A4	Jordan et al. "Heparin promotes 237(4816):777-9.	the inactivation of antithro	mbin by neutrophil elastase." Science. 1987		
Examiner Signature	o: Da	te Considered:			

Examiner Signature:	Date Considered:	
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not		

considered. Include copy of this form with next communication to applicant.

25 NOV 2005

ATTORNEY DOCKET NO. 21101.0021U2 APPLICATION NO. 10/516,662 SHEET 3 OF 4

INFORMATION	DISCLOSURE STATEMENT	Application Number	Complete if Known 10/516,662
INFORMATION	LIST	Filing Date	June 2, 2003
LIST		First Named Inventor	Bock et al.
(Use as	nany sheets as necessary)	Group Art Unit	Unassigned
(333,33	,,,	· ·	
		Examiner Name	Unassigned
A44			of the heparin-dependent anticoagulant
	mechanism." Arch. Biochem. Bio		
A45	69 <sup>th</sup> Scientific Sessions, Abstract	4336, 1996 94:8 Supp., p	
A46	Kocsis et al. "Heparin-coated ster	nts." J. Long-Term Effects	s of Medical Implants. 2000 10:19-45.
A47	15(2):373-7.		beta by antithrombin III." Biochemistry. 1976
A48	critically ill patients with suspecte 1984 82(4):396-404.	d disseminated intravasc	n III, C1(-)-inhibitor and alpha 2-macroglobulin in ular coagulation (DIC)." Am. J. Clin. Pathol.
A49	Lawson et al. "Complex-depende 1993 268(2):767-70.	ent inhibition of factor VIIa	by antithrombin III and heparin." J. Biol. Chem.
, A50	Mammen et al. "Human antithron coagulation." Semin. Thromb. He		perimental disseminated intravascular .
A51	Mant et al. "Haemorrhagic compl		
A52	Marcum et al. "Microvascular hep Pt 1):H725-33.	parin-like species with ant	icoagulant activity." Am. J. Physiol. 1983 245(5
A53	Minnema et al. "Recombinant human antithrombin III improves survival and attenuates inflammatory responses in baboons lethally challenged with Escherichia coli." Blood. 2000 95(4):1117-23.		
A54	Mizuochi et al. "Structural studies of the carbohydrate moiety of human antithrombin III." Arch. Biochem. Biophys. <b>1980</b> 203(1):458-65.		
A55	Nakajima et al., "Mapping the extended substrate binding site of cathepsin G and human leukocyte elastase," J. Biol. Chem. 1979 254:4027.		
A56	Nuijens et al. "Plasma elastase a mediators in fatal sepsis." J. Lab.		toferrin in sepsis: evidence for neutrophils as 159-68.
A57			ormation of the serpin antithrombin." Science.
A58			appa B activation in human monocytes and
A59	Olson et al. "Identification of critic	al molecular interactions	mediating heparin activation of antithrombin. ants." Trends Cardiovasc. Med. <b>2002</b> 12:198-
A60		of the antithrombin confo	ride in heparin acceleration of antithrombin- rmational change contribution to heparin rate
A61	Ostrovsky et al. "Antithrombin III prevents and rapidly reverses leukocyte recruitment in ischemia/reperfusion." Circulation. 1997 96(7):2302-10.		
A62	Owen et al." P1 variant antithrom increased heparin affinity and are activation mechanism." FEBS Let	bins Glasgow (393 Arg to resistant to catalytic clea tt. <b>1991</b> 280(2):216-20.	His) and Pescara (393 Arg to Pro) have avage by elastase. Implications for the heparin
A63	antitrypsin and antithrombin-III." Telsevier/North Holland Biomedica	The Physiological Inhibito al Press. 1979 pp. 43-54.	rin cofactor) – partial homology between α1- rs of Coagulation and Fibrinolysis,
A64	Peterson and Blackburn, "Isolation and characterization of an antithrombin III variant with reduced carbohydrate content and enhanced heparin binding." J. Biol. Chem. 1985 260(1):610-5.		

Examiner Signature:	Date Considered:	
EXAMINER: Initial if reference considered, w considered. Include copy of this form with next co	nether or not citation is in conformance with MPEP 609; Draw line through citation if not mmunication to applicant.	in conformance and not

Reg'd PCT/PTO 25 NOV 2005

ATTORNEY DOCKET NO. 21101.0021U2 APPLICATION NO. 10/516,662 SHEET 4 OF 4

INFOP	MATION D	ISCLOSURE STATEMENT	Application Number	Complete if Known 10/516,662
INFORMATION DISCLOSURE STATEMENT		Filing Date	June 2, 2003	
LIST			First Named Inventor	Bock et al.
	(Use as m	any sheets as necessary)		
	(000 00 111		Group Art Unit	Unassigned
			Examiner Name	Unassigned
	A65	Picard and Bock, "Rapid and effic	cient one-tube PCR-base	d mutagenesis method." Methods in Mol. Biol.
		Totowa, NJ, 1996, 183-8.		genetic engineering. B.A. White Humana Press
	A66	polymerase." Nucleic Acid Res. 1	994 22(13):2587-91.	utagenesis technique using Pfu DNA
	A67	position of its N-glycosylation con antithrombin III isoform with enha	agine-135 is caused by the serine in the third responsible for production of the beta-ochemistry. <b>1995</b> 34(26):8433-40.	
	A68	Rao et al. "Binding of factor VIIa t VIIa." Blood. 1993 81(10):2600-7		pid antithrombin III/heparin inhibition of factor
	A69	cofactor." J. Biol. Chem. 1973 24	8(18):6490-505.	of action of human antithrombin-heparin
	A70	Rosenberg, "Chemistry of the her Proc. <b>1977</b> 36(1):10-8.	mostatic mechanism and	its relationship to the action of heparin." Fed.
	A71	Rothenburger et al. "Treatment o		ociated with theMicroMed DeBakey VAD using 12 106(suppl I): I-189-92.
	A72	recombinant tissue plasminogen activator." Circulation 2002 106(suppl I): I-189-92.  Ruf and Mueller, "Tissue factor in cancer angiogenesis and metastasis." Curr. Opin. Hematol. 1996 3(5):379-84.		
	A73	Seitz et al. "Participation and interactions of neutrophil elastase in haemostatic disorders of patients with severe infections." Eur. J. Haematol. <b>1987</b> 38(3):231-40.		
	A74	Stephens et al. "Site directed mutagenesis of the reactive center (serine 394) of antithrombin III." J. Biol. Chem. <b>1988</b> 263(31):15849-52.		
	A75	Tani et al. "Thrombin enhances lu J. Respir. Cell Mol. Biol. 1991 5(1		n in bleomycin-induced pulmonary fibrosis." Am
	A76	Tejada, M.L. and Deeley, R.G. "C	loning of an avian antithr	ombin: developmental and hormonal regulation
	A77	of expression." Thromb. Haemost. 1995 73(4):654-661.  Turk et al. "The oligosaccharide side chain on Asn-135 of alpha-antithrombin, absent in beta-antithrombin decreases the heparin affinity of the inhibitor by affecting the heparin-induced conformational change." Biochemistry: 1997 36(22):6682-91.		
	A78	Uchiba et al. "Antithrombin III (AT III) prevents LPS-induced pulmonary vascular injury: novel biological activity of AT III." Semin. Thromb. Hemost. <b>1997</b> 23(6):583-90.		
	A79			ency states." Semin. Hematol. <b>1997</b> 34(3):188-
	A80	Varga et al. "Infectious entry path	way of adenovirus type 2	2." J. Virol. 1991 65(11):6061-70.
	A81	Vinazzer, "Antithrombin III in shoot Thrombosis/Hemostasis. 1995 1:	ck and disseminated intra	vascular coagulation." Clin. Appl.
	A82			a randomized controlled trial." JAMA. 2001
	A83	Witmer and Hatton, "Antithrombing	III-beta associates more aortic wall in vitro and in	readily than antithrombin III-alpha with vivo." Arteriosclerosis and Thrombosis. 1991
	A84	Wolff et al. "Direct gene transfer i	nto mouse muscle in vivo	o." Science. 1990 247(4949 Pt 1):1465-8.
	A85	Zendehrouh, Ph.D. Dissertation,	'Novel proteinase inhibito	ors for use in treatment of sepsis." Temple Univ f Michigan dissertation archive in 1999.

Examiner Signature:	Date Considered:
EXAMINER: Initial if reference considered, whether or not cit	ation is in conformance with MPEP 609: Draw line through citation if not in conformance and not

considered. Include copy of this form with next communication to applicant.